amended to remove "http://" from all website addresses throughout the specification. No new matter enters by these amendments. Support for these amendments may be found throughout the specification and the figures including, for example, page 1 lines 21-23, page 8 lines 10-12, page 15 lines 13-14, and page 46 lines 19-28.

I. Election/Restrictions

Applicants maintain that the election requirement is improper. The Office Action states that the election requirement remains proper because "...the search and consideration are different for each Group since a different search would be performed...." Office Action at page 2. However, Applicants maintain that the complete examination of the application would be handled most expeditiously by treating all of the pending claims as a single entity. As Section 803 of the MPEP directs, "[i]f the search and examination of an entire application can be made without serious burden, the Office must examine it on the merits, even though it includes claims to distinct or independent inventions." To facilitate prosecution, however, Applicants have elected claims 1-10, 13, 20, 22, 91 and 92 and the species of Signal Sequence 3 and G-CSF and acknowledge that the requirement is made final. As such, non-elected Claims 11, 12, 14-19, 21, and 23-90 have been cancelled without prejudice or disclaimer to the underlying subject matter.

Applicants strenuously disagree with the Office's contention that Applicants' argument "appears to be an admission that the species are obvious variants of one another." Office Action mailed August 6, 2002 at page 2. The Office has requested that Applicants "clearly state on the record that the species are not patentably distinct and are obvious variants of one another." Office Action mailed August 6, 2002 at page 2.

Applicants have not admitted in the Response to Restriction Requirement and do not now admit that the species are obvious variants. After all, each species of a genus may be patentably distinct, yet pose no additional burden on the Examiner to examine all of the species. *See* MPEP § 803(A) and (B).

II. Rejections under 35 U.S.C. § 102(e)

Claims 1-7, 9, 10, 13, 20, 91, and 92 were rejected under 35 U.S.C. §102 (e) as being anticipated by Lee et al (U.S. Patent Number 6,020,169) (hereinafter "Lee"). Office Action mailed August 6, 2002 at page 3. However, in order to support an anticipation rejection under 35 U.S.C. §102, the Examiner must demonstrate that each and every element of a claimed invention is disclosed within a single prior art reference. *In re Bond*, 15 U.S.P.Q.2d 1566, 1567 (Fed. Cir. 1990). Indeed, the reference must describe an applicant's claimed invention sufficiently to have placed a person of ordinary skill in the art in the field of the invention in possession of it. *See In re Paulson,* 31 U.S.P.Q.2d 1671 (Fed. Cir. 1994).

Regarding independent claim 1 and claims dependent thereon, Lee is deficient as an anticipatory reference because whatever else it may teach or suggest, Lee fails to teach or suggest the accumulation of the expressed cytokine to a level greater than 1% of the total soluble protein (TSP). The Office states that clone 81 of the Lee reference "produced over 1000 ng IL-4 per gram of Calli, which inherently represents more than 1% of the total soluble protein." Office Action mailed August 6, 2002 at page 4. However, Applicants respectfully submit that the Office's comparison of amount of cytokine per gram of Calli to amount of cytokine per total soluble protein is inappropriate

and is akin to comparing apples to oranges. Moreover, Applicants respectfully submit that no basis has been provided for the Office's suggestion that 1000 ng IL-4 per gram of Calli inherently represents more than 1% of the total soluble protein. To establish inherency "the Office must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990). The Office has not provided any such technical reasoning or scientific fact, and thus has not met this burden of proof.

Moreover, to establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference. *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999); *see also Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347 (Fed. Cir. 1999); *Abbott Laboratories v. Geneva Pharmaceuticals, Inc.*, 182 F.3d 1315 (Fed. Cir. 1999). To be found inherent in an anticipating reference, an unstated element must exist as a matter of scientific fact and flow naturally from the elements expressly disclosed in the prior art reference. *Hughes Aircraft Co. v. U.S.*, 8 USPQ2d 1580, 1583 (Ct. Cl. 1988). The Lee reference fails to meet these requirements.

The Office also asserts that Lee "expressly teaches that expression of over 1% of total protein is achievable." Office Action mailed August 6, 2002 at page 4. Applicants respectfully disagree. Lee states that "...coexpression of both chains led to a large accumulation of antibody within the leaf tissue, an increase from 0.3% to 1.3% of the total leaf protein." (emphasis added). Lee *et al.* at column 1, lines 44-46. Whatever else

Lee may teach or suggest, it does not teach or suggest a cytokine accumulating to a level greater than 1% of the total soluble protein. Thus, the Lee reference thus fails to disclose each and every limitation of the claimed invention. Because Lee does not teach all elements of Claims 1-7, 9, 10, 13, and 20, Applicants respectfully submit that Lee does not anticipate the claims.

The Examiner further alleges that claim 91 is anticipated by Lee et al. Claim 91 relates to a methodology for the production of a cytokine that is free from amino acid modifications. The Examiner alleges that "Lee teaches a method for producing a cytokine...which is free from amino acid modification." Office Action mailed August 6, 2002 at page 3. Applicants respectfully traverse this rejection.

Whatever else it may teach or suggest, Lee fails to teach or suggest production of a cytokine that is free from amino acid modifications. Referring to Figure 13 of the Lee reference, the Office states that "IL-4 has [the] same molecular weight as recombinant human IL-4." Apparently, on this basis, the Office concludes that the recombinant IL-4 protein is free from amino acid modifications. However, Applicants respectfully point out that a Western blot is insufficient to conclude whether or not a protein is free from amino acid modifications because it does not reveal the amino acid composition or structure of a protein. Because Lee fails to teach all of the elements of Claim 91, Applicants submit that Lee does not anticipate Claim 91.

The Office also alleges that claim 92 is anticipated by Lee. The Office alleges that "Lee teaches a method for producing a cytokine...which is free from novel glycosylation." Office Action mailed August 6, 2002 at page 3. Applicants respectfully

disagree. Lee is not an anticipatory reference because whatever else Lee may teach or suggest, Lee fails to teach production of a cytokine that is free from novel glycosylation. The Examiner argues that Figure 13 of Lee demonstrates that the recombinant IL-4 protein is free from novel glycosylation. However, Figure 13 of Lee is a Western blot and as such is insufficient to conclude that the IL-4 protein is free from novel glycosylation. Because Lee does not teach all of the elements of Claim 92, Applicants submit that Lee does not anticipate Claim 92.

Thus, on the basis of the foregoing, Applicants respectfully request withdrawal of the rejections of Claims 1-7, 9, 10, 13, 20, 91, and 92 under 35 U.S.C. §102 (e).

III. Rejections under 35 USC § 103

Claims 8 and 22 were rejected under 35 U.S.C. §103 (a). Applicants respectfully traverse these rejections.

The Office alleges that claim 22 is rejected under 35 USC § 103 as being unpatentable over Lee in view of Boone. Office Action mailed August 6, 2002 at page 5.

As previously discussed, Lee is deficient as a primary reference because it fails to teach or suggest each and every limitation of independent claim 1 upon which Claim 22 depends. Lee fails to teach or suggest, for example, the accumulation of an expressed cytokine to a level greater than 1% of the total soluble protein (TSP).

The Office has argued that Boone teaches "expression of G-CSF in plants", but this does not remedy Lee's deficiencies. The law requires that an anticipatory reference must teach or suggest all of the claim limitations. *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442

(Fed. Cir. 1991). Neither Lee nor Boone teaches or suggests the accumulation of an expressed cytokine to a level greater than 1% of the total soluble protein. Hence, the cited references taken alone or in combination do not teach, suggest, or make obvious the present invention.

The Office alleges that claim 8 is rejected under 35 USC § 103 as being unpatentable over Lee in view of Schouten. Office Action mailed August 6, 2002 at page 7. The Office has argued that Schouten teaches "expression of G-CSF in plants", but this does not remedy Lee's deficiencies. The law requires that an anticipatory reference must teach or suggest all of the claim limitations. *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). Neither Lee nor Schouten teaches or suggests the accumulation of an expressed cytokine to a level greater than 1% of the total soluble protein. Hence, the cited references taken alone or in combination do not teach, suggest, or make obvious the present invention.

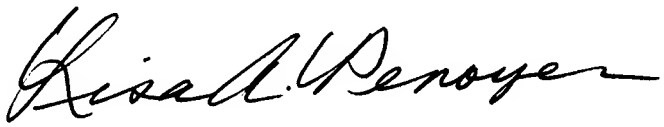
Accordingly, on the basis of the foregoing, Applicants respectfully request that the rejection of Claims 8 and 22 under 35 U.S.C. §103 be withdrawn.

CONCLUSION

It is believed that the present claims are in immediate condition for allowance. Accordingly, Applicants respectfully request that the Examiner pass the application to issue. In the event that any extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned. Applicants do not believe any additional fees are due in conjunction with this filing. However, if any

fees under 37 C.F.R. §§ 1.16 or 1.17 are required in the present application, including any fees for extensions of time, then the Commissioner is hereby authorized to charge such fees to Arnold & Porter Deposit Account No. 50-2387, referencing matter number 18337.006.

Respectfully submitted,



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Marked up version

IN THE SPECIFICATION:

At page 17, line 5:

The present invention also contemplates producing biologically active, authentic granulocyte colony stimulating factor (G-CSF) from a plant host system. G-CSF is an O-glycosylated 19 kDa glycoprotein, and the biologically active form is a monomer. cDNA analysis of G-CSF has revealed a protein of 207 amino acids containing a hydrophobic secretory signal sequence of 30 amino acids. Furthermore, G-CSF contains 5 cysteine residues, four of which form disulfide bonds. The sugar moiety of G-CSF is not required for full biological activity. *G-CSF*, Cytokines Online Pathfinder Encyclopedia [(http://www.](www-copewithcytokines.de/). A particular therapeutic product is produced from mammalian cells, with 174 amino acids, the native N-terminus and mammalian-type O-glycosylation. Ono et al., 30A(3) EUR. J. CANCER S7-S11 (1994). A product is also produced from bacterial cells, with 175 amino acids, a non-native methionine at the N-terminus, and no glycosylation. PHYSICIAN'S DESK REFERENCE (2000).

IN THE CLAIMS:

1. (Amended) A method for producing a cytokine in a plant host system wherein said plant host system has been transformed with a [chimeric]nucleic acid sequence encoding said cytokine, comprising the steps of:

cultivating said transformed plant host system under the appropriate conditions to result in the expression of said cytokine in said plant host system

wherein said cytokine accumulates to a level greater than 1% of the total soluble protein in a sample of said plant host system.

91. (Amended) A method for producing a cytokine in a plant host system wherein said plant host system has been transformed with a [chimeric]nucleic acid sequence encoding a cytokine, comprising the step of:

cultivating said transformed plant host system under the appropriate conditions to result in the expression of said cytokine, wherein said expressed cytokine is free from amino acid modifications[in said plant host system].

92. (Amended) A method for producing a cytokine in a plant host system wherein said plant host system has been transformed with a [chimeric]nucleic acid sequence encoding a cytokine, comprising the step of:

cultivating said transformed plant host system under the appropriate conditions to result in expression of said cytokine, wherein said expressed cytokine is free **from** novel glycosylation[in said plant host system].